turnal paralysis but did not appear to influence his course. Paralytic episodes ceased in both patients after they became euthyroid on propylthiouracil therapy and have not recurred following successful radioactive iodine ablation. Finally, although paralysis is no longer apparent, the intrinsic defect remains and paralysis will recur with either recurring Graves' or iatrogenic hyperthyroidism.[21,22]

Due to the rare familial appearance of this disorder, we obtained human leukocyte antigen studies and compared them with previous reports in the literature. The following antigens were shared by both brothers: A24, B13, Bw4, Cw3, DR2, DQw1. Tamai and co-workers in a large population of male Japanese patients found DRw8 to be significantly more prevalent in patients with thyrotoxic periodic paralysis compared with patients with only Graves' disease.[23] Yeo and associates found A2, B40, Bw22, and Bw46 to be shared by two Chinese with thyrotoxic paralysis.[24] Kelly and Fishman reported a black man with A23, B14, and B15.[25] Valenta and colleagues similarly found A23 in a black woman with the disorder.[26] It appears that no histocompatibility antigen is universally associated with this disorder despite isolated reports suggesting some association in specific races.

REFERENCES

1. Rosenfeld M: Acute aufsteigende lähmungbei. Morbus Basedow, Berl Klin Wochenschr 1902; 39:538

2. Shinosaki T: Klinische studien ueber die periodische extremitatenlahmung. Z Gesamte Neurol Psychiatr 1926; 100:564-611

3. Talbot JH: Periodic paralysis. Medicine (Baltimore) 1941; 20:85-143

4. McFadzean AJS, Yeung R: Familial occurrence of thyrotoxic periodic paralysis. Br Med J 1969; 1:760

5. Leung AKC: Familial 'hashitoxic' periodic paralysis. J R Soc Med 1985; 78:638-640

6. Norris FH: Status of the segmental ennervation in thyrotoxic periodic paralysis. Electroencephalogr Clin Neurophysiol 1966; 21:67-70

7. Engel AG: Electron microscopic observations in primary hypokalemic and thyrotoxic periodic paralysis. Mayo Clin Proc 1966; 41:797-808

8. McFadzean AJS, Yeung R: Periodic paralysis complicating thyrotoxicosis in Chinese. Br Med J 1967; 1:451-455

9. Okinada S, Shizume K, Watanabe A, et al: The association of periodic paralysis and hyperthyroidism in Japan. J Clin Endocrinol Metab 1957; 17:1454-1459

10. Shy GM, Wanko T, Rowley PT, et al: Studies in familial periodic paralysis. Exp Neurol 1961; 3:53-121

11. Hofmann WW, Smith RA: Hypokalemic periodic paralysis studies in vitro. Brain 1970; 93:445-474

12. Norris FH, Clark EC, Biglieri EG: Studies in thyrotoxic periodic paralysis. J Neurol Sci 1971; 13:431-442

13. Engel AG, Lambert EH: Calcium activation of electrically inexcitable muscle fibers in primary hypokalemic periodic paralysis. Neurology (Minneap) 1969; 19:851-858

14. Gordon AM, Green JR, Lagunoff D: Studies on a patient with hypokalemic familial periodic paralysis. Am J Med 1970; 48:185-195

15. McArdle B: Metabolic myopathies. Am J Med 1963; 35:661-672

16. Samuels MA: Manual of Neurologic Therapeutics: With Essentials of Diagnosis. Boston, Little, Brown, 1978

17. Griggs RC, Engel WK, Resnick JS: Acetazolamide treatment of hypokalemic periodic paralysis—Prevention of attacks and improvement of persistent weakness. Ann Intern Med 1970; 73:39-48

18. Yeung RTT, Tse TE: Thyrotoxic periodic paralysis—Effect of propranolol. Am J Med 1974; 57:584-590

19. Conway MJ, Seibel JA, Eaton RP: Thyrotoxicosis and periodic paralysis—Improvement with beta blockade. Ann Intern Med 1974; 81:332-336

20. Williams ME, Gervino EV, Rosa RM, et al: Catecholamine modulation of rapid potassium shifts during exercise. N Engl J Med 1985; 312:823-827

21. Robertson EG: Thyrotoxic periodic paralysis. Aust NZ J Med 1954; 3:182

22. Okihiro MM, Nordyke RA: Hypokalemic periodic paralysis—Experimental precipitation with sodium liothyronine. JAMA 1966; 198:949-951

23. Tamai H, Tanaka K, Komaki G, et al: HLA and thyrotoxic periodic paralysis in Japanese patients. J Clin Endocrinol Metab 1987; 64:1075-1078

24. Yeo PPB, Chan SH, Lui KF, et al: HLA and thyrotoxic periodic paralysis. Br Med J 1978; 2:930

25. Kelly TM, Fishman LM: Thyrotoxic periodic paralysis in a black male. J Endocrinol Invest 1984; 7:517-519

26. Valenta LJ, Treadwell T, Berry R, et al: Idiopathic thrombocytopenic purpura and Graves disease. Am J Hematol 1982; 12:69-72

Paraneoplastic Cerebellar Degeneration Due to Hodgkin's Disease

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PARANEOPLASTIC CEREBELLAR DEGENERATION is a rare yet well-described consequence of systemic malignancy. Seen most commonly in tumors of the lung and ovary, it may also complicate the course of cancers of the breast, uterus, stomach, colon, and larynx. It was first described pathologically in Hodgkin's lymphomas by Malamud.[1(p302)] Progressive ataxia, vertigo, nystagmus, and dysarthria are its clinical hallmarks.[2]

We report the case of a patient who had a pure cerebellar syndrome as the sole manifestation of Hodgkin's disease. He was treated with conventional radiation therapy, and his neurologic syndrome abated dramatically. In a review of previously reported cases that had clinical data available, we found only one other case of such a dramatic improvement after therapy.[3]

Report of a Case

A previously healthy 31-year-old man presented in March 1986 because for the past two weeks he had had vertical diplopia and "vibrating vision" on left lateral gaze. He had had no previous illnesses or hospital admissions. He was taking no medications and his family history was negative. A review of systems was notable for slurring of speech and oscillopsia. In addition, the patient complained of general clumsiness and an unsteady gait.

The results of the general physical examination were unremarkable except for a palpable lymph node in the left supraclavicular fossa. On neurologic examination he had bilateral, horizontal, gaze-evoked nystagmus, with an upbeat component on gaze to the left. On cerebellar testing he had a pronounced intention tremor and dysdiadochokinesia of the left upper extremity and bilateral oscillation with the heel-to-shin maneuver. His gait was wide-based and unsteady, and his speech was mildly dysarthric.

Laboratory tests showed normal values for the hemogram, erythrocyte sedimentation rate, electrolytes, and liver and renal function tests. Assays for fluorescent antinuclear antibody and rheumatoid factor were negative. A serum protein electrophoresis was normal. The fluorescent treponemal antibody test was nonreactive. Serum titers for viral and

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ABBREVIATIONS USED IN TEXT
CSF = cerebrospinal fluid
CT = computed tomographic
MRI = magnetic resonance imaging

fungal pathogens were negative. An enzyme-linked immunosorbent assay for antibody to the human immunodeficiency virus was negative. A skin anergy panel was reactive, and the chest roentgenogram was normal.

Computed tomographic (CT) and magnetic resonance imaging (MRI) scans of the head showed no evidence of cerebellar atrophy. Brain-stem auditory-evoked responses, visual-evoked responses, and an electroencephalogram were normal. The cerebrospinal fluid (CSF) was under normal pressure with a glucose level of 3.3 mmol per liter (60 mg per dl) and a protein level of 490 mg per liter (49 mg per dl). The leukocyte count showed 35×10^6 per liter (0.14 segmented neutrophils, 0.81 lymphocytes, and 0.05 histiocytes), but a cytologic examination showed no malignant cells. A VDRL test for syphilis was nonreactive, and myelin basic protein was absent. The results of CSF electrophoresis were normal, with an immunoglobulin G index of 0.21 (normal, less than 0.25). All cultures, stains, and smears were negative.

Two months after his presentation, on May 29, 1986, a biopsy of the left scalene lymph node revealed nodular sclerosing Hodgkin's disease. A staging evaluation—including CT scans of the chest, abdomen, and pelvis; lymphangiography; bone marrow biopsy; and staging laparotomy—established that the patient's lymphoma was at stage II.

The patient underwent a course of standard radiation therapy (mantle and para-aortic). On follow-up neurologic examination two months later in July 1986, he still had the previously noted nystagmus; the tremor, dysdiadochokinesia, and gait problems, however, were totally resolved. The CSF findings had improved dramatically (see Table 1), and the cytologic examinations again did not show malignant cells. Specimens of CSF and serum were screened for anti-Purkinje cell antibody at the Mayo Clinic medical laboratory using an indirect immunofluorescence technique; these results were negative. Serial analyses of CSF for glucose, protein, and cell counts are summarized in Table 1. All viral, bacterial, and fungal cultures were persistently negative. Likewise, malignant cells were never found in the CSF.

TABLE 1.—*Laboratory Analysis of Cerebrospinal Fluid From Serial Lumbar Punctures*

Component	*3/5/86*	*5/12/86*	*5/19/86*	*5/27/86*	*7/25/86*
Protein, mg/liter*	600	560	490	360	380
Glucose, mmol/liter†	2.9	2.9	3.3	3.1	3.2
Cell count × 10^6/liter (differential cell fractions)	28 (0.41 segmented neutrophils, 0.5 lymphocytes, 0.08 monocytes, 0.01 bands)	104 (0.1 segmented neutrophils, 0.77 lymphocytes, 0.13 monocytes)	35 (0.14 segmented neutrophils, 0.81 lymphocytes, 0.05 histiocytes)	42 (0.04 segmented neutrophils, 0.88 lymphocytes, 0.08 monocytes)	5 (1.00 lymphocytes)

*Normal value, 450 mg/liter.
†Normal value is two thirds of serum glucose value, or 2.8 to 4.4 mmol/liter.

TABLE 2.—*Clinical and Laboratory Data on Previously Reported Cases of Paraneoplastic Cerebellar Degeneration*

Source	*No. of Cases*	*Cerebrospinal Fluid*		*APCA*	*Imaging Studies*	*Syndrome Duration Before Hodgkin's Disease Diagnosed, mo*	*Cerebellar Signs Respond to Treatment*
		*Cellularity, ×10^6/liter**	*Globulin*				
Malamud, 1974[1]	1	NR	NR	NR	NR	NR	No
Froissart et al, 1976[3]	1	12 (1.00 lymphocytes)	"Normal"	NR	NR	9	Yes
Brazis et al, 1981[5]	1	9 (1.00 lymphocytes)	"Normal"	NR	Cerebellar atrophy on CT	10	NR
Horwich et al, 1966[6]	1	1 (unspecified)	NR	NR	NR	4	No
Trotter et al, 1976[7]	1	2 (1.00 monocytes)	"Normal"	Present	NR	6	No
Tsapatsaris et al, 1979[8]	1	243 (0.87 lymphocytes)	NR	NR	Normal	2-3	No
Rewcastle, 1963[9]	1	"Acellular"	NR	NR	NR	5	NR
Ludmerer and Kissane, et al, 1985[10]	1	"Normal"	NR	NR	Normal	4-5	NR
Cunningham et al, 1986[11]	5	NR	NR	Absent	NR	NR	NR
Jaeckle et al, 1983[12]	1	NR	NR	NR	NR	NR	NR
Brain and Wilkinson, 1965[13]	1	6 (1.00 lymphocytes)	NR	NR	NR	8†	NR
Croft and Wilkinson, 1969[14]	1	NR	NR	NR	NR	NR	NR
Valtysson et al, 1979[15]	1	6 (1.00 mononuclear)	"Normal"	NR	Normal	17	No
Victor and Ferendelli, 1970[16]	1	"Normal"	"First zone elevation of gum mastic curve"	NR	NR	2-3†	NR
Present case	1	35 (0.14 segmented neutrophils, 0.81 lymphocytes, 0.05 histiocytes)	"Normal"	Absent	CT normal, MRI normal	3	Yes

APCA=anti-Purkinje cell antibody, CT=computed tomography, MRI=magnetic resonance imaging, NR=not reported

*The figures in parentheses represent differential cell fractions.
†Years.

Discussion

This patient's clinical presentation is typical of paraneoplastic cerebellar degeneration with Hodgkin's disease. The pathogenesis of this disorder is unclear, but possible mechanisms include the production of toxic factor(s) by the primary malignant disease, viral infection, abnormal populations of leukocytes with neurotoxic effects, or antibodies that cross-react with tumor and neuronal antigens.[2,4]

Although rare, paraneoplastic cerebellar degeneration caused by Hodgkin's disease is well documented.[3,5-16] In Table 2 is a list of reported cases and available clinical data.

Several aspects of this case bear emphasis. First, few patients who have this disorder caused by Hodgkin's disease have responded to treatment of the underlying lymphoma. Froissart and co-workers reported the remarkable response of their patient to treatment with mechlorethamine hydrochloride (mustard), vincristine sulfate (Oncovin), prednisone, and procarbazine hydrochloride.[3] Other patients have shown either a steady progression of cerebellar signs or at best a halt in progression.

Second, the presence of anti-Purkinje cell antibody in patients who have paraneoplastic cerebellar degeneration due to systemic malignancy has been documented primarily in carcinoma of the breast and ovary.[2,7,11,12] Although one case of this antibody occurring in a patient with Hodgkin's disease has been reported,[7] the report was criticized by several authors because serum diluted to less than 1:100 results in nonspecific staining.[11] The negative result in our case would support the findings of most of the reports on the subject.

Third, we did not find any other report of MRI studies on patients with this disorder, although CT was done on four patients. The normal results from CT and MRI in our patient no doubt reflect the early diagnosis and treatment of his lymphoma (stage II disease) before cerebellar atrophy became prominent. This early treatment would also explain his good therapeutic response because pathologic specimens of paraneoplastic cerebellar degeneration in advanced disease have shown extensive loss of Purkinje cells and thinning of the granule cell and molecular layers.[9,13,16]

Fourth, other authors have not reported polymorphonuclear cells in the CSF.[3,5-10,13,15,16] The pronounced pleocytosis of the CSF in our patient cannot easily be explained. The patient was afebrile, we saw no "left shift" on the hemogram, and no paraspinal focus was evident. Notably, the change from polymorphonuclear forms to lymphocytes occurred without antibiotic therapy—this finding argues against an infectious cause. Tsapatsaris and colleagues reported 0.87 lymphocytes in their patient but did not comment on the remaining cell types.[8]

Finally, we recommend that patients who present with a florid cerebellar syndrome and a paucity of other physical signs should have a careful examination of the lymphatic system.

REFERENCES

1. Malamud N: Atlas of Neuropathology. Berkeley, University of California Press, 1974

2. Greenlee JE, Brashear R: Antibodies to cerebellar Purkinje cells in patients with paraneoplastic cerebellar degeneration and ovarian carcinoma. Ann Neurol 1983; 14:609-613

3. Froissart M, Mizon JP, Morcamp D, et al: Atrophie cérébelleuse subaiguë paranéoplasique au cours d'une maladie de Hodgkin. Nouve Presse Med 1976; 5:2549-2550

4. Ang LC, Zochodne DW, Ebers GC, et al: Severe cerebellar degeneration in a patient with T-cell lymphoma. Acta Neuropathol (Berl) 1986; 69:171-175

5. Brazis PW, Biller J, Fine M, et al: Cerebellar degeneration with Hodgkin's disease—Computed tomographic correlation and literature review. Arch Neurol 1981; 38:253-256

6. Horwich L, Buxton PH, Ryan GMS: Cerebellar degeneration with Hodgkin's disease. J Neurol Neurosurg Psychiatry 1966; 29:45-51

7. Trotter JL, Hendin BA, Osterland CK: Cerebellar degeneration with Hodgkin disease—An immunological study. Arch Neurol 1976; 33:660-661

8. Tsapatsaris N, Wanger SL, Steinberg D: Cerebellar degeneration and Hodgkin's disease. Arch Intern Med 1979; 139:829-830

9. Rewcastle NB: Subacute cerebellar degeneration with Hodgkin's disease. Arch Neurol 1963; 9:407-413

10. Ludmerer KM, Kissane JM: Cerebellar dysfunction and nephrotic syndrome in a 50-year-old man. Am J Med 1985; 79:621-627

11. Cunningham J, Graus F, Anderson N, et al: Partial characterization of the Purkinje cell antigens in paraneoplastic cerebellar degeneration. Neurology 1986; 36:1163-1168

12. Jaeckle KA, Houghton AN, Nielsen SL, et al: Demonstration of serum anti-Purkinje antibody in paraneoplastic cerebellar degeneration and preliminary antigenic characterization (Abstr). Ann Neurol 1983; 14:111

13. Brain L, Wilkinson M: Subacute cerebellar degeneration associated with neoplasms. Brain 1965; 88:465-478

14. Croft PB, Wilkinson M: The course and prognosis in some types of carcinomatous neuromyopathy. Brain 1969; 92:1-8

15. Valtysson G, Fisher-Beckfield P, Carbone PP: Cerebellar degeneration with Hodgkin's disease. CA 1979; 29:246-249

16. Victor M, Ferendelli JA: The nutritional and metabolic diseases of the cerebellum—Clinical and pathological aspects, *In* Fields WS, Willis WD (Eds): The Cerebellum in Health and Disease. St Louis, Warren H. Green, 1970, pp 412-449